els of B-Type natriuretic peptide despite significantly increased LV mass and volumes, even in patients with symptoms. Therefore, BNP may not be a useful marker in the management and evaluation of patients with chronic MR.

ORAL CONTRIBUTIONS

841 Clinical Markers Predictive of Outcome in Patients With Valvular Heart Disease

Tuesday, April 01, 2003, 8:30 a.m.-10:00 a.m.
McCormick Place, Room S101

8:30 a.m.

841-1 The Effective Regurgitant Orifice Area Is Predictive of Survival in Patients With Organic Mitral Regurgitation

Maurice L. Enriquez-Sarano, A. Jamil Tajik, David Messika-Zeitoun, Jean-Francois Avierinos, Michael Bellamy, Christophe Tribouilloy, Mayo Clinic, Rochester, MN

Background: Quantitation of mitral regurgitation (MR) is possible using Doppler-Echocardiography and allows measurement of the Effective Regurgitant orifice (ERO) area and of the Regurgitant volume (RVol). However, the implications of these measurements regarding survival after diagnosis are unknown because no long-term study outcome study has yet been conducted.
Methods: We prospectively enrolled 458 patients with MR due to organic mitral lesions (mitral prolapse in 360 or 79%) in whom quantitation of MR was obtained at baseline by at least 2 independent methods. The end-points analyzed were survival under conservative management and the combined end-point of death or mitral surgery.
Results: At diagnosis, age was 64±14 years and 61% were male, ERO was 41±28 mm2 (range 2 to 180 mm2) and RVol was 65±40 mL/beat (range 3 to 227). The left ventricular end-diastolic volume was enlarged at 107±28 mL/m2 and the ejection fraction was normal at 69±9%. The 5-year rates of mortality under conservative management and of surgery or death were 24±3% and 66±3%. Both ERO and RVol were univariately predictive of these end-points (P<0.001) but in multivariate analysis adjusting for age, sex, functional class and ejection fraction, only ERO was predictive of survival (RR 1.22 [1.06-1.38] per 10 mm2 increase, P=0.005). ERO was also independently predictive of death or mitral surgery (RR 1.41 [1.29-1.52] per 10 mm2 increase, P<0.001). 5 years after diagnosis, for patients with ERO<20, 20-30 and ≥30 mm3, mortality under conservative management was 9±3%, 31±10% and 49±8%, respectively and death or mitral surgery (excluding patients operated within 3 months of diagnosis) was 14±4%, 55±9% and 83±4%, respectively (both P<0.001).
Conclusion: The present study demonstrates for the first time in patients with organic MR, 1-the strong outcome implications of quantitative measures of degree of MR, 2-the preeminent independent prognostic value for survival of ERO area, which 3-allows to stratify patients into groups at low-, medium- and high-risk. Hence, measurement of ERO area of MR is an essential tool in management of patients with organic MR.

8:45 a.m.

841-2 Brain Natriuretic Peptide Predicts Severity of Aortic Stenosis

Johann Auer, Thomas Weber, Robert Berent, Elisabeth Lassnig, Josef Seier, Bernd Eber, General Hospital Wels, Wels, Austria

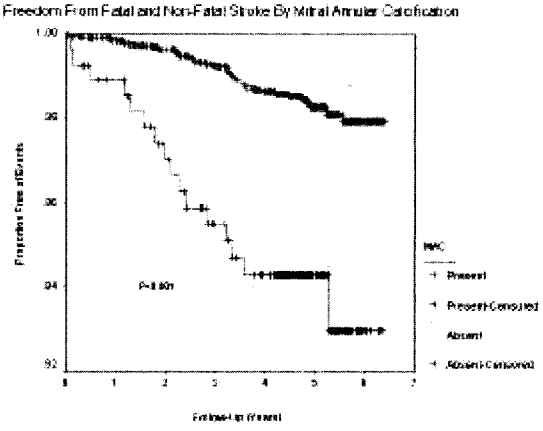
Background: Brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) constitute a cardiac hormone system mediating natriuresis, diuresis, and vasodilation. Whereas ANP is secreted mainly from cardiac atria, BNP is produced to a larger extent in ventricles and has been shown to correlate with end-systolic wall stress in patients with aortic stenosis (AS). Echocardiography with doppler examination of the aortic valve provides a very accurate assessment of the trans-valvular aortic pressure gradient (TVPG) and is used to monitor progression of AS. This study evaluated circulating BNP as a marker of left ventricular hypertrophy and atrial pressure increase in patients with AS.
Patients and Methods: We investigated the serum concentrations of BNP by radioimmunoassay in 69 AS patients (35 males, mean age 70,9 years; range 37-90; mean TVPG determined by echocardiography 45,2 mmHg (+/- 20,6), calculated mean aortic valve area (AVA) (assessed invasively) 0,85 cm2 (+/- 0,3). TVPG were correlated to the AVA (r=0,54, P=0,001). Results are expressed as mean (+/- standard deviation), correlations were tested by Spearman-rang test and comparisons between group were tested by the Mann-Whitney test.
Results: BNP levels were significantly higher in AS patients with AVA less than 1 cm2 (2558,5 pg/ml; +/- 2555,6) when compared with the patients with AVA more than 1 cm2 (1567,4 pg/ml (+/- 2447,9) P=0,049). Moreover, BNP levels were increased in AS patients with TVPG of 50 (60,5 +/- 10,3) mmHg or more (4351,4 pg/ml; +/- 4699,5) in comparison to patients with TVPG less than 50 (29,9 +/- 16,6) mmHg (1373,8 pg/ml; +/- 2178,8, P=0,04). BNP levels were correlated to the TVPG and AVA (r=0.43 and r=0.52, P<0.001), respectively.
Conclusion: These results suggest BNP levels increase in relation to the TVPG and AVA. BNP measurement could potentially be used to monitor progression of disease non-invasively. This marker may also be useful to identify the optimum time for surgery in AS.

9:00 a.m.

841-3 Mitral Annular Calcification, Aortic Sclerosis, and Incident Stroke in American Indians Free of Clinical Cardiovascular Disease

Jorge R. Kizer, David O. Wiebers, Jack P. Whisnant, James M. Galloway, Thomas K. Welty, Elisa T. Lee, Lyle Best, Mary J. Roman, Richard B. Devereux, Weill Medical College of Cornell University, New York, NY, Mayo Clinic, Rochester, MN

While mitral annular calcification (MAC) & aortic sclerosis have been reported to be risk factors for cerebrovascular events, their relative prognostic significance independent of other echo predictors is uncertain. We investigated the predictive value of MAC & aortic sclerosis for incident stroke while accounting for other proven echo predictors. Our cohort comprised American Indians in the Strong Heart Study having echo in 1993-95. Exclusion criteria: coronary/valvular disease (aortic stenosis); prior stroke; atrial fibrillation; ejection fraction ≤ 35%; segmental wall motion abnormality. Follow-up was obtained through 12/99. N = 2859. Age = 58 y, women = 64%, hypertension = 54%, diabetes = 47%, cholesterol/HDL = 4.7, body-mass index = 31 kg/m^2, smoker = 31%, renal insufficiency = 2.3%, MAC = 10%, aortic sclerosis = 8%, left atrial index = 2.2 cm/m, LV mass index = 40 g/m$^{2.7}$. Incident strokes = 60. MAC, but not aortic sclerosis, was a significant univariable predictor of stroke (Figure). In Cox models adjusting for all above factors, MAC emerged as an independent predictor of stroke (RR 2.2, P = 0.028). Aortic sclerosis was not predictive whether or not MAC was considered. Our findings demonstrate MAC to be a strong predictor of stroke independent of other echo risk factors, & are in line with other studies showing that aortic sclerosis is not independently predictive of cerebral events. In patients without overt cardiovascular disease, the isolated presence of MAC warrants aggressive primary prevention.



9:15 a.m.

841-4 Does Aortic Valve Sclerosis Predict Cardiovascular Events Independently of Albuminuria in Hypertension? A LIFE Study

Michael H. Olsen, Kristian Wachtell, Jonathan N. Bella, Vittorio Palmieri, Eva Gerdts, Markku S. Nieminen, Gunnar Smith, Björn Dahlöf, Hans Ibsen, Richard B. Devereux, Glostrup University Hospital, Copenhagen, Denmark, The Weill Medical College of Cornell University, New York, NY

Background: Aortic valve (AV) sclerosis and albuminuria are strong cardiovascular risk factors and they are both thought to be markers of atherosclerosis. In the LIFE study we investigated the predictive value of AV sclerosis for the composite endpoint (CEP) of cardiovascular death, non-fatal stroke or non-fatal myocardial infarction correcting for urine albumin/creatinine ratio (UACR) and other cardiovascular risk factors.
Methods: After two weeks of placebo treatment, clinical, laboratory, and echocardiographic variables were assessed in 960 hypertensive patients from the LIFE Echo substudy, aged 55-80 (mean 66±7) years, with electrocardiographic LV hypertrophy, and without known AV stenosis. Morning urine albumin and creatinine were measured, and urine albumin-creatinine ratio (UACR) was calculated. Macro- and microalbuminuria were defined as UACR≥35 and 3.5≤UACR<35, respectively. AV sclerosis was defined as valve thickening or calcification. 15 patients with mild AV stenosis were excluded.
Results: AV sclerosis was found in 388 patients and was associated with higher incidence of CEP (15.5% vs. 8.3%**). Micro- and macroalbuminuria were found in 143 (17.1%) and 23 (2.8%) patients, respectively, and both were associated with higher incidence of CEP (15% and 22% vs. 9.9%*). The incidence of CEP increased progressively with micro- and macroalbuminuria in patients without AV sclerosis (11.4% and 15.4% vs. 8.3%*) as well as in patients with AV sclerosis (19.2% and 30% vs. 12.7%*). In Cox regression analyses AV sclerosis was predictive of the CEP (odds ratio [OR] = 1.6*) independent of log UACR (1.5*); male gender (2.1**); and history of peripheral vascular disease (2.5**), diabetes mellitus (2.3**) or cerebral vascular disease (2.4**). *P<0.05.